Nootropil®

GlaxoSmithKline

Piracetam

NAME OF THE MEDICINAL PRODUCT

Nootropil 1g/ 5ml for intravenous use.
NOOTROPIL 3 g/15 ml solution for intravenous injection
NOOTROPIL 12 g/60 ml solution for infusion

QUALITATIVE AND QUANTITATIVE COMPOSITION

NOOTROPIL 1 g/5 ml solution for intravenous injection: Each 5 ml vial contains 1 g of Piracetam
NOOTROPIL 3 g/15 ml solution for intravenous injection: Each 15 ml vial contains 3 g of Piracetam
NOOTROPIL 12 g/60 ml solution for infusion: Each 60 ml vial contains 12 g of Piracetam
(See List of Excipients)

PHARMACEUTICAL FORM

1 g / 5ml, 3 g/15ml solution for injection and 12 g/60ml solution for infusion: clear colourless solution

CLINICAL PARTICULARS

Therapeutic indications

Mild cognitive deterioration in the elderly.

Posology and method of administration:

Infusion: one 12 g infusion bottle a day.
Intravenous use: 1-2 vial a day.
The dose can be doubled.
The high bioavailability of the substance causes identical therapeutic effects in orally and intravenously administered Piracetam. Therefore oral administration is recommended in patients under long term treatment and those presenting intravenous administration problems.
Duration and posology must, anyhow, be adjusted by the attending doctor, depending on each case.

Contra-indications

Hypersensitivity to piracetam or other pyrrolidone derivatives or any of the excipients.
Piracetam is contra-indicated in patients with cerebral haemorrhage.
Piracetam is contra-indicated in End Stage Renal Disease patients.
Piracetam should not be used in patients suffering from Huntington's Chorea.

Special warnings and special precautions for use

Due to the platelet antiaggregant effect of piracetam, caution is recommended in patients with severe haemorrhage, patients at risk of bleeding such as gastrointestinal ulcer, patients with underlying disorders of haemostasis, patients with history of haemorrhagic CVA, patients undergoing major surgery including dental surgery, and patients using anticoagulants or platelet antiaggregant drugs including low dose aspirin.
Piracetam is eliminated via the kidneys and care should thus be taken in cases of renal insufficiency.
For long-term treatment in the elderly, regular evaluation of the creatinine clearance is required to allow dosage adaptation if needed.
Abrupt discontinuation of treatment should be avoided in myoclonic patients as this may induce sudden relapse or withdrawal seizures.
Warnings related to the excipients:

- Sodium:
  Piracetam 3g/15ml solution for injection: This product contains less than 1 mmol (23mg) sodium per 24 g piracetam.
  Piracetam 12g/60ml solution for infusion: This product contains about 19 mmol (or about 445 mg) sodium per 24 g piracetam.
  To be taken into consideration by patients on a controlled sodium diet.

Interaction with other medicinal products and other forms of interaction

Confusion, irritability and sleep disorder have been reported during concomitant treatment with thyroid extract (T3 + T4). In a published single-blind study on patients with severe recurrent venous thrombosis, piracetam 9.6 g/d did not modify the doses of acenocoumarol necessary to reach INR 2.5 to 3.5, but compared with the effects of acenocoumarol alone, the addition of piracetam 9.6 g/d significantly decreased platelet aggregation, β-thromboglobulin release, levels of fibrinogen and von Willebrand's factors (VIII : C; VIII : vW : Ag; VIII : vW : RCo) and whole blood and plasma viscosity.
The drug interaction potential resulting in changes of piracetam pharmacokinetics is expected to be low because approximately 90% of the dose of piracetam is excreted in the urine as unchanged drug.
In vitro, piracetam does not inhibit the human liver cytochrome P450 isoforms CYP 1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1 and 4A9/11 at concentrations of 142, 426 and 1422 µg/ml.
At 1422 µg/ml, minor inhibitory effects on CYP 2A6 (21%) and 3A4/5 (11%) were observed. However, the Ki values for inhibition of these two CYP isoforms are likely to be well in excess of 1422 µg/ml. Therefore, metabolic interaction of piracetam with other drugs is unlikely.
A 20 g daily dose of piracetam over 4 weeks did not modify the peak and trough serum levels of antiepileptic drugs (carbamazepine, phenytoin, phenobarbitone, valproate) in epileptic patients who were receiving stable doses.
Concomitant administration of alcohol had no effect on piracetam serum levels and alcohol levels were not modified by a 1.6 g oral dose of piracetam.

Pregnancy and lactation

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal / foetal development, parturition or post-natal development. There are no adequate data from the use of piracetam in pregnant women. Piracetam crosses the placental barrier. Drug levels in the newborn are approximately 70% to 90% of maternal levels. Piracetam should not be used during pregnancy unless clearly necessary. Piracetam is excreted in human breast milk. Therefore, piracetam should be avoided during breastfeeding or breastfeeding should be discontinued, while receiving treatment with piracetam.

Effects on ability to drive and use machines

Given the adverse events observed with the drug, an influence on driving and using machines is possible and should be taken into account.

Undesirable effects

Clinical studies

Double-blind placebo-controlled clinical or pharmacoclinical trials, of which quantified safety data are available (extracted from the UCB Documentation Data Bank on June 1997), included more than 3000 subjects receiving piracetam, regardless of indication, dosage form, daily dosage or population characteristics.
When adverse events are grouped together according to WHO System Organ Classes, the following classes were found to be related to a statistically significantly higher occurrence under treatment with piracetam:

- psychiatric disorders
- central and peripheral nervous system disorders
- metabolic and nutritional disorders
- body as a whole- general disorders.

The following adverse experiences were reported for piracetam with a statistically significantly higher incidence than placebo. Incidences are given for piracetam (n = 3017) versus placebo (n = 2850) treated patients.

WHO System Organ Class	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)
Nervous system disorders	Hyperkinesia (1.72 vs. 0.42%)	
Metabolism and nutrition disorders	Weight increased (1.29 vs. 0.39%)	
Psychiatric disorders	Nervousness (1.13 vs. 0.25%)	Somnolence (0.96 vs. 0.25%) Depression (0.83 vs. 0.21%)
General disorders and administration site conditions		Asthenia (0.23 vs. 0.00%)

Post-marketing experience

From the post-marketing experience, the following additional adverse drug reactions have been reported (sorted according to MedDRA System Organ Classes). Data are insufficient to support an estimate of their incidence in the population to be treated.
Blood and Lymphatic disorders: haemorrhagic disorder
Ear and labyrinth disorders: vertigo
Gastrointestinal disorders: abdominal pain, abdominal pain upper, diarrhoea, nausea, vomiting
Immune system disorders: anaphylactoid reaction, hypersensitivity
Nervous system disorders: ataxia, balance impaired, epilepsy aggravated, headache, insomnia
Psychiatric disorders: agitation, anxiety, confusion, hallucination
Skin and subcutaneous tissue disorders: angioneurotic oedema, dermatitis, pruritus, urticaria
Rare cases of injection site pain, thrombophlebitis, pyrexia or hypotension have been reported after intravenous administration.

Overdose

Symptoms

One case of bloody diarrhoea with abdominal pain, associated with the oral intake of 75 g piracetam daily, was most probably related to the extreme high dose of sorbitol contained in the used formulation.
No other case was reported that would point to additional adverse events specifically related to overdose.

Management of overdose

In acute, significant overdosage, the stomach may be emptied by gastric lavage or by induction of emesis. There is no specific antidote for overdose with piracetam. Treatment for an overdose will be symptomatic treatment and may include hemodialysis. The extraction efficiency of the dialyser is 50 to 60% for piracetam.

PHARMACEUTICAL PARTICULARS

List of excipients

Piracetam 1 g/5 ml solution for injection: Sodium acetate - Glacial acetic acid - Water for injections.
Piracetam 3 g/15 ml solution for injection: Sodium acetate - Glacial acetic acid - Water for injections.
Piracetam 12 g/60 ml solution for infusion: Sodium acetate - Glacial acetic acid - Sodium chloride - Water for injections.

Incompatibilities

None known.

Shelf life

As indicated on the outer packaging

Special precautions for storage

Store below 25 °C

Nature and contents of container

Solution for injection: transparent glass vials.
Solution for infusion: transparent glass bottle closed by a rubber closure made of chlorobutyl elastomer.

Instruction for use/handling

No special requirements

Manufactured by:

UCB Pharma S.p.A., Pianezza, Italy
For GlaxoSmithKline Export Limited

CCDS Piracetam (C2010-012), Effective: 28 August 2010

THIS IS A MEDICAMENT

- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The Doctor and the Pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your Doctor.

Keep medicament out of reach of children

Council of Arab Health Ministers
Union of Arab Pharmacists
CIA74341A